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EXHIBIT A

REPEAT OF EXAMPLE 8 FROM U.S. PATENT NO.
5,643,575.

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Experiment 1.

Purpose: To repeat Example 8 from U.S. Patent 5,643,575 and examine the purity of the recrystallized product.

I. Materials:

Methoxy-PEG-nitrophenyl carbonate (mPEG-5K-NPC), MW 5240 daltons, was prepared following a standard procedure (Lot Number PT-038-15). L-lysine ethyl ester, dihydrochloride salt, was purchased from Sigma, MW 247.2. Pyridine was purchased from Aldrich and used without further purification.

II. Method:

A mixture of 5.46 g (1.0 mmol) of mPEG-5K-NPC, 150 mg (0.6 mmol) of L-lysine ethyl ester dihydrochloride and 143 microliters (1.8 mmol) of pyridine was refluxed in 100 mL of dichloromethane (DCM) for 22 hours under an inert argon atmosphere. The solvent was evaporated at 40 °C using a rotary evaporator. The remaining residue was recrystallized from 200 mL of 2-propanol. The recrystallized product was recovered by filtration, rinsed with 50 mL of 2-propanol, and dried under high vacuum.

III. Results:

Yield: 5.20 g (95%). The recovered product was analyzed by ^1H NMR (FIG. 1). The NMR revealed that the recrystallized material contained no "U-LYS-PEG", but rather corresponded to unreacted starting material, mPEG-5K-NPC.

In looking at FIG. 1, the top ^1H NMR spectrum a) is of the starting material, mPEG-5K-NPC, and the bottom ^1H NMR spectrum b), although plotted to a slightly different scale, is of recrystallized product. As can be seen by comparing the two plots, both correspond to the same material, as evidenced by the reported chemical shift values.

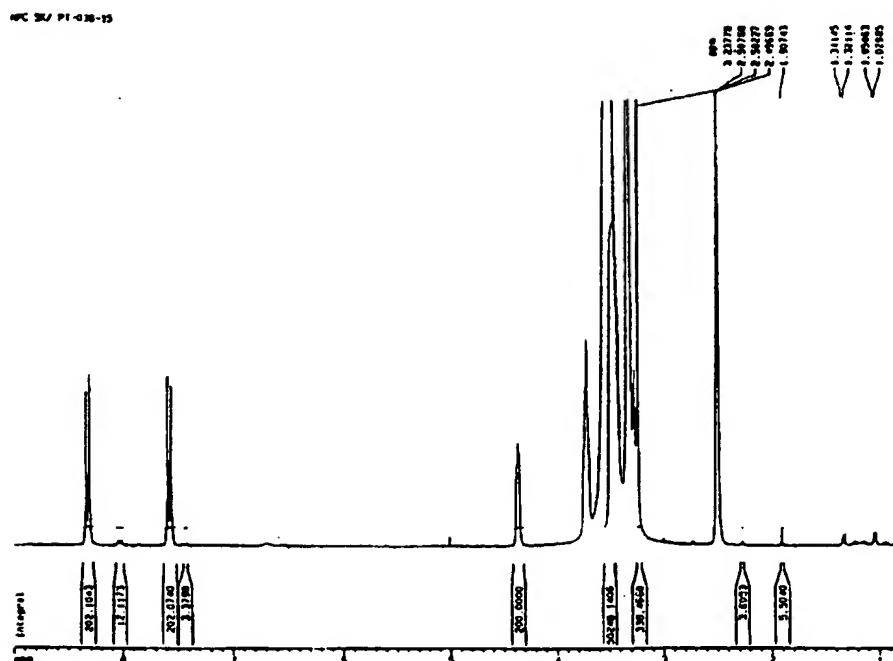
IV. Conclusion:

An effort to repeat Example 8 of the '575 patent resulted not in the reported U-LYS-PEG branched polymer product but instead resulted in recovery of unreacted polymer starting material. In sum, the reaction did not work. Therefore, an examination of the stringency of the reported purification method, recrystallization, in removing polymeric impurities could not be conducted based upon a straightforward repeat of Example 8 of the '575 patent.

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a)



b)

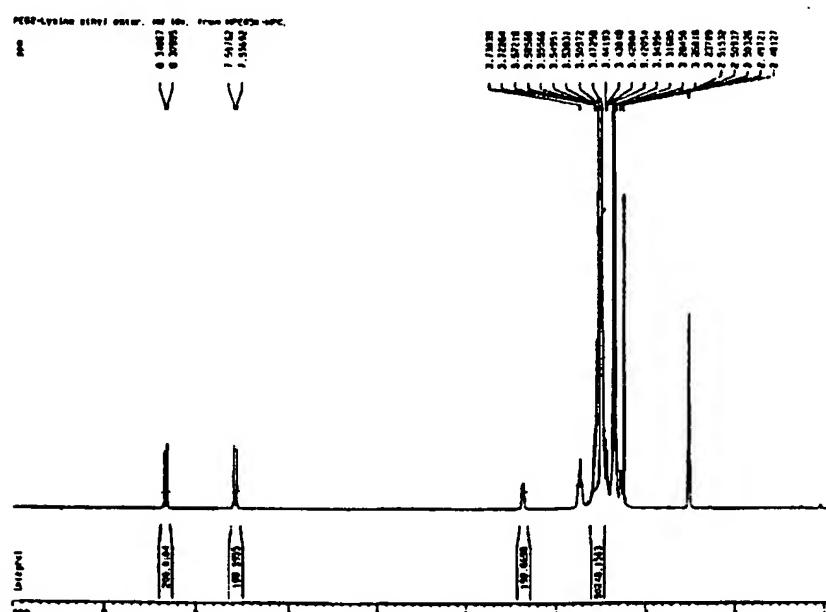


FIG. 1 ¹H-NMR of a) MPEG5k-NPC b) The reaction product of MPEG5k-NPC and L-lysine ethyl ester dihydrochloride in this preparation. MPEG5k-NPC remains unreacted.